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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/446,145	01/07/00	MIYAKE H	0018-1086-PC

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1624	8

DATE MAILED: 07/19/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/446,145	Hiroshi Miyake et al.
Examiner	**Group Art Unit**
Sudhaker Patel	1624

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) 1-10 is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-10 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Applicants communication paper # 6 dated 6/19/00 is acknowledged.

Claims 1-10 are pending in this application.

The traversal is on the ground(s) that the restriction is not proper because the required search is not burdensome. This is not persuasive because the compounds according to the pending claims are drawn to structurally dissimilar compounds having different components on to the 1,3 diazine ring, and thus represent different chemical structures/formulae for claimed Formula (I) as already outlined in earlier Office Action. They are structurally dissimilar such that a reference anticipating a compound may not render the remaining compounds obvious e.g. combinations like I).diazine-piperazine -phenyl; v.s. ii). diazine-pyridazine-phenyl; v.s. iii).diazine-piperazine-piperazine; iv). diazine-piperidine-piperazine and others. 37 CFR 1.141(a) provides that two or more independent and distinct inventions may not be claimed in one application, whether or not the misjoinder occurred in one claim or more than one claim. Restriction is going to be exercised where independent and distinct inventions are presented in one Markush grouping. Independent means when the compound is being made and/or used alone, not in combination with other compounds of the Markush expression. Restriction is considered proper in Markush claims where the members are so diverse and unrelated that a prior art reference anticipating the claim with respect to one of the members, would not render the claims obvious under 35 U.S.C. 103 with respect to the other members. Therefore, what should be considered for the patentable

distinctness is the compound as a whole. The examination by PTO takes into consideration the whole molecule for classification and examination purposes. The compounds as identified in the groups are classified separately and require separate searches in the literature and therefore, it is burdensome for the examiner. If a reference for one would not be a reference for the other, then restriction is considered proper.

The inventions listed as Groups I-VI do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Pursuant to 37 C.F.R. 1.475 (d), the ISA/US considers that where multiple products and processes are claimed, the main invention shall consist of the first invention of the category first mentioned in the claims and the first recited invention of each of the other categories related thereto. Accordingly, the main invention (Group I) comprises the first recited product. Further, pursuant to 37 C.F.R. 1.475 (d), the ISA/US considers that any feature which the subsequently recited products and methods share with the main invention does not constitute a special technical feature within the meaning of PCT Rule 13.2 and that each of such products and methods accordingly defines a separate invention.

Restriction is proper where there is lack of unity of invention and such is not affected by the manner of claiming i.e. in separate claims or within a single claim. Note 37 CFR 1.141 (a) which states two or more independent, distinct inventions may not be claimed in one application. One application includes the possibility of the separate inventions appearing in one claim or more

than one claim. This is also consistent with PCT Rule 13.3 for PCT cases entering the national stage.

Thus, the restriction is still deemed proper and is therefore made ***FINAL***.

Applicants have elected **Group I** with traverse and have also elected species of working example compound 73-(2) on page 151 of the specification, which is ***(2R)-1-(3,5-Bis(trifluoromethyl)benxoyl)-4-(4-(3S)-3-ethylmorpholino)-2-butynyl)-2-((1H-indol-3-yl)methyl)piuperazine dihydrochloride***. Since claims 1-10 link with other inventions, such claims and the application will be examined with regard to the subject matter of invention of **Group I** only as elected, and mentioned in above quoted communication #6 of 6.19/00. Affirmation of this election must be made by the applicants in replying to this Office Action.

Specification

1. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves

modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

Claim Rejections - 35 U.S.C. § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/use the invention.

1). In evaluating the enablement question, several factors are to be considered. In re Wands, 8 USPQ 2d 1400 (Fed. Cir. 1988); Ex parte Forman, 230 USPQ 546. The factors include:***(1).*** The nature of invention;***(2).*** the state of prior art ;***(3).*** the predictability or lack thereof in the art; ***(4).***

the amount of direction or guidance present;*(5).* the presence or absence of working examples;*(6).* the breadth of the claims, and *(7).* the quantity of experimentation needed.

The nature of the invention in the instant case has generic claims which embrace a wide range of chemically and physically distinct compounds wherein applicants claim different types of "compounds" *with multiple options for - R1,R2, R3, R4 groups* presented by various meanings in a very generic ***Formula*** as presented in claim 1. These groups could be further (un)substituted by more than one substituent(s) which are independently selected from the group consisting of various hetero rings etc. and furthermore together with various provisos for R4 & R1 form various molecules for the instant compounds are not described in the disclosure in such a way that one of ordinary skill in the art would know how to prepare the various compounds suggested by the claims. Rings &/or various group(s) either substituted &/or unsubstituted embraced by other group(s) e.g. homomorpholinylamino(lower) alkyl; saturated heterocyclicaminocarbonyl(lower)alkyl/(lower)alkoxy(lower)alkyl each of which may have substituent(s) in Formula of claim 1, are not enabled as they read on rings/groups having multiple heteroatoms.

Most of the compounds made and tested are based on only examples having general structure = Substituted Benzene-C0-((1,4-diazine)indole)- linked to either a heterocycle(pyridine/morpholine/thiomorpholine) via aliphatic C3-4 chain containing a triple bond -etc. as claimed in the generic claim 1 representing Formula. In view of the lack of direction provided in the specification regarding starting material sources for forming derivatives

of various groups/cyclic rings involving hetero atoms with substitutents as generically claimed together with the relative scarcity of working examples, and general unpredictability of chemical reactions, it would take an undue amount of experimentation for one skilled in the art to make the claimed compounds and therefore practice the invention. See Ex parte Moersch, 104 USPO 122; In re Howarth, 210 USPO 689; In re Lund 153 USPO 625; In re Wiggins, 179 USPO 421.

Furthermore, there's no reasonable basis for assuming that the myriad of compounds embraced by the generic claims will all share the same pharmacological/physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for using such compounds having heterocyclic ring with R4 representing ar(lower)alkoxycarbonyl; which may have 1-3 substituent(s) selected from the group consisting of mono(or di or tri)halo(lower)alkyl and halogen including bu not limited to "Spirocyclic" group for treating or preventing a patient with disorders selected from but not limited to Substance P-mediated diseases, ophthalmic diseases, Inflammatory diseases, food allergy, cardiac failure, AIDS related dementia, Alzheimer's diseases, Parkinson's diseases, herpes zoster, and other disorders (in a mammal/human) by either instantly claimed compounds alone &/or in combination with an additional adjutants/suspending agents that enhance stability of the active component. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush

group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as pharmaceutical art.

On pages 32-34 applicants have tried to describe some important Biological assays for instantly claimed compounds, but there is no relevant test/assay data with/without inclusion of art recognized compounds proving the novelty and superior performance of the instantly claimed. compounds. Therefore, a comparison can not be made at a glance for the unexpected results by the instant claims. On page 33 applicants have simply presented "Test Results" for compounds which include elected species Example 73-(2) for inhibition rate of 125 I-BH-Substance P binding to h-NK1. On page 34, 5 selected compounds' "profile of Emesis in ferret" are presented, but have not included the species of Example 73-(2).However, applicants do not correlate the results of various tests for compounds as claimed.

However, the applicants do not provide comparative results/assays to support their claimed novel compounds' performance for human beings

Applicants are also requested to note that Application Serial #s; 09545614; 09356684; 09238187; and others involving either one or more of the inventors, and similar subject matter to current application are located thru' preliminary search. These references are in transit and are not accessible to the examiner at this time. Applicants are advised to provide the information related to similar &/or presently pending local or international applications, if any, related to the subject matter included in the instant application to avoid various issues arising out of question of either double patenting &/or priority claims and other related legal matters.

This application has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicants' cooperation is, therefore, requested in promptly correcting any errors of which they may become aware in the specification.

Preliminary computer assisted search revealed following reference/ publications:

EP 655442

W0 9722597

Note, both of the references teach making of piperazine-derivative including Aroyl-derivatives for using them as tachykinin antagonists. These references are cited here but not used at this stage.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sudhaker Patel whose telephone number is (703) 308 4709. The examiner can normally be reached on Monday thru' Friday from 8:30 AM to 5:00 PM. If attempts to reach the examiner by the phone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached at (703) 308 4716.

A facsimile center has been established for Group 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4556 or (703) 305-3592.

Any inquiry of general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308 1235.

Mukund J. Shah

Mukund Shah

Supervisory Patent Examiner

Art Unit 1624.

sp

July 15, 2000